

# Physical functioning and quality of life after cancer rehabilitation

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In order to overcome cancer-related problems and to improve quality of life, an intensive multi-focus rehabilitation programme for cancer patients was developed. We hypothesised that this six-week intensive rehabilitation programme would result in physiological improvements and improvement in quality of life. Thirty-four patients with cancer-related physical and psychosocial problems were the subjects of a prospective observational study. A six-week intensive multi-focus rehabilitation programme consisted of four components: individual exercise, sports, psycho-education, and information. Measurements (symptom-limited bicycle ergometry performance, muscle force and quality of life [RAND-36, RSCL, MFI]) were performed before (T0) and after six weeks of rehabilitation (T1). After the intensive rehabilitation programme, statistically significant improvements were found in symptom-limited bicycle ergometry performance, muscle force, and several domains of the RAND-36, RSCL and MFI. The six-week intensive multi-focus rehabilitation programme had immediate beneficial effects on physiological variables, on quality of life and on fatigue.

Zur Überwindung krebserkrankter Probleme und zur Verbesserung der Lebensqualität wurde für Tumorkranken ein intensives Mehrkomponenten-Rehabilitationsprogramm entwickelt. Wir stellten die Hypothese auf, dass dieses sechswöchige intensive Rehabilitationsprogramm zu Verbesserungen des körperlichen Zustands und der Lebensqualität führen würde. 34 Patienten mit krebserkrankten physischen und psychosozialen Problemen. Ort der Prüfung: Rehabilitationszentrum. Studiendesign: Prospektive Beobachtungsstudie. Intervention: Ein aus vier Komponenten bestehendes, sechswöchiges intensives Rehabilitationsprogramm mit individuellem Belastungstraining, Sport, psychologischer Betreuung und Patientenschulung. Messparameter: Symptombegrenzte Fahrradergometrie, Muskelkraft und Lebensqualität (RAND-36, RSCL, MFI). Die Messungen erfolgten vor (T0) und nach der sechswöchigen Rehabilitation (T1). Nach Absolvieren des intensiven Rehabilitationsprogramms waren statistisch signifikante Verbesserungen bei der Symptombegrenzten Fahrradergometrie, der Muskelkraft und mehreren Parametern von RAND-36, RSCL und MFI festzustellen. Das sechswöchige intensive Mehrkomponenten-Rehabilitationsprogramm wirkte sich unmittelbar günstig auf physiologische Variablen, die Lebensqualität sowie Müdigkeit und Abgeschlagenheit aus.

Con el fin de superar los problemas relacionados con el cáncer y mejorar la calidad de vida, se desarrolló un programa de rehabilitación multifocal intensiva para pacientes oncológicos. Nuestra hipótesis era que un programa de rehabilitación intensiva de seis semanas de duración se traduciría en mejorías fisiológicas y de la calidad de vida. Treinta y cuatro pacientes con problemas físicos y psicosociales relacionados con el cáncer. *Ámbito:* Centro de rehabilitación. *Diseño:* Estudio observacional prospectivo. *Intervención:* Un programa de rehabilitación multifocal intensiva de seis semanas constituido por cuatro componentes: ejercicio individual, deportes, psicoeducación e información. *Criterios de valoración:* Ejercicio en bicicleta ergométrica limitado por los síntomas, fuerza muscular y calidad de vida (RAND-36, RSCL y MFI). Las mediciones se hicieron antes (T0) y después de seis semanas de rehabilitación (T1). Después del programa de rehabilitación intensiva se observaron mejorías estadísticamente significativas en el ejercicio en bicicleta ergométrica limitado por los síntomas, en la fuerza muscular y en varios dominios del RAND-36, RSCL y MFI. El programa de rehabilitación multifocal intensiva de seis semanas tuvo efectos beneficiosos inmediatos sobre las variables fisiológicas, la calidad de vida y la fatiga.

Afin de surmonter les problèmes liés au cancer et améliorer la qualité de vie des patients atteints d'un cancer, un programme de rééducation intensif comportant plusieurs facettes a été élaboré. Nous avons pris pour hypothèse qu'un programme de rééducation intensif de six semaines apporterait des améliorations sur le plan physiologique et sur le plan de la qualité de vie. 34 patients souffrant de problèmes physiques et psychosociaux liés au cancer. *Cadre:* Centre de rééducation. *Conception:* Etude complémentaire par observation. *Intervention:* Un programme de rééducation intensif de six semaines comprenant quatre facettes: exercices individuels, sport, psychopédagogie et information. *Indicateurs des résultats:* performance sur bicyclette ergométrique limitée par les symptômes, force musculaire et qualité de vie (RAND-36, RSCL, MFI). Les mesures ont été prises avant (T0) et après les six semaines de rééducation (T1). A l'issue du programme de rééducation intensif, des améliorations significatives ont été observées dans la performance sur bicyclette ergométrique limitée par les symptômes, la force musculaire et dans plusieurs

domaines du RAND-36, du RSCL et du MFI. Le programme de rééducation intensif comportant plusieurs facettes a eu des effets favorables immédiats sur les variables physiologiques, la qualité de vie et la fatigue. *International Journal of Rehabilitation Research* 27:27-35 © 2004 Lippincott Williams & Wilkins.

International Journal of Rehabilitation Research 2004, 27:27-35

## Introduction

Cancer and the treatment of cancer are often associated with impaired physical capacity and psychosocial problems and can therefore substantially diminish quality of life (Bjorndal *et al.*, 1995). Impaired physical capacity can be explained by several factors, such as tumour toxicity and the treatment of cancer (Seifert *et al.*, 1992)—including surgery, chemotherapy and radiotherapy—which may induce cardiorespiratory and muscular-skeletal deconditioning. Impaired physical capacity may lead to a greater degree of exertion being required for the performance of everyday activities. Consequently, patients may experience fatigue even when performing normal activities. Patients are usually advised to avoid physical exertion and to minimize their daily activity load in order to reduce fatigue. As a result, a vicious circle of fatigue, reduced activity and further impaired physical capacity may occur. Impaired physical capacity has been postulated as being a substantial contributor to cancer-related fatigue (Winningham, 1991) and to diminished quality of life in cancer patients (Dimeo *et al.*, 1997).

Cancer patients may also experience psychosocial problems. The psychosocial problems most frequently mentioned are anxiety, depression, mood disturbances, stress, insecurity, grief and decreased self-esteem (Argerakis, 1990; Body *et al.*, 1997; De-Boer *et al.*, 1999; Delbruck *et al.*, 1993; Fallowfield *et al.*, 1993; Ganz *et al.*, 1992; Hill *et al.*, 1992; Schwibbe, 1991). Additionally, problems in job reintegration and social isolation are reported in cancer patients (Anderson, 2002).

Several rehabilitation programmes have been developed, consisting of physical or psychological interventions to overcome the cancer-related physical and psychosocial problems and to improve quality of life in cancer patients. Physical exercise training is thought to be beneficial for cancer patients in promoting health, reducing or preventing cancer-related fatigue and improving quality of life (Courneya and Friedenreich, 2000; Courneya *et al.*, 2000; Dimeo *et al.*, 1996; 1997; MacVicar *et al.*, 1989; Pinto *et al.*, 1999; Schwartz, 1998; Seifert *et al.*, 1992; Winningham, 1991; Young McCaughan & Sexton, 1991). However, very little data supporting this hypothesis has been gathered to date.

**Keywords:** rehabilitation, physiological variables, quality of life, fatigue, cancer patients

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Psychosocial interventions for cancer patients can be divided into three general categories (Bloom & Kessler, 1994): (1) coping-skills training based on cognitive-behavioural approaches, (2) patient education and (3) support groups. It has been demonstrated that these psychosocial interventions can facilitate coping with the disease and potentially improve quality of life (Anderson, 2002; Cunningham & Edmonds, 1996; Fawzy *et al.*, 1993; Greer *et al.*, 1992; Hill *et al.*, 1992; Hitch *et al.*, 1994; Trijsburg *et al.*, 1992).

Physical and psychological interventions may be combined in multi-focus rehabilitation programmes. Berglund *et al.* (1994a; 1994b) evaluated a multi-focus rehabilitation programme consisting of low-intensity physical training, and information and coping-skills training in a selected group of patients with breast cancer. The study revealed perceived physical benefits in addition to psychosocial benefits, although the latter were only quantified with a questionnaire and not with physiological measures. Berglund's results were confirmed by another study on 14 selected patients with breast cancer during chemotherapy (Mock *et al.*, 1994). These studies suggested that multi-focus rehabilitation programmes are beneficial to breast cancer patients. However, it is unclear whether these programmes are feasible and effective in unselected mixed groups of cancer patients.

For the present study, we developed a cancer rehabilitation programme for a mixed group of cancer patients based on three theoretical assumptions. Firstly, we acknowledged the value of Engel's bio-psychosocial model (Engel, 1997), which, in our opinion, requires a multi-focus approach. We accordingly developed a multi-focus programme including psychosocial, educational and physical interventions. Secondly, the intervention consisted of an intensive rehabilitation period of six weeks with a large number of contact hours. We expected this boost programme to have positive and immediate effects on physical and psychosocial outcomes. Thirdly, with respect to the physical part of the intervention, we theorized that genuine physiological improvements might be key to breaking the vicious circle of impaired physical capacity, fatigue and reduced activity. Consequent to the expectation of the inclusion of cancer patients with low

physical capacity and a high level of fatigue, we developed a mild-to-moderate training programme of six weeks that would be both feasible and effective in improving physiological functioning. If a short, boost programme were to produce an improvement in both physiological functioning and quality of life, it might eventually contribute to the further development of cancer rehabilitation programmes. Therefore, it was of the utmost importance to determine both effects at approximately six weeks, i.e., at the end of the intensive rehabilitation programme.

The purpose of this study was to evaluate the immediate effects of the intensive multi-focus rehabilitation programme on physiological variables and on quality of life in cancer patients. We hypothesized (1) that the intensive multi-focus programme would result in physiological training effects, and (2) that the intensive multi-focus programme would result in an improvement of quality of life and a decrease of fatigue.

## Patients and methods

### Patients

The rehabilitation programme was developed for cancer patients who experienced impaired physical and psychosocial functioning after cancer treatment. The programme was open to patients referred by hospitals and by general practitioners. Participants were included in the programme and study if they met the following inclusion criteria:

- Age > 18 years
- Last cancer-related treatment > three months ago
- Life expectancy  $\geq$  one year
- An indication for rehabilitation, e.g., patients were included in the programme if they met at least three of the following criteria, as judged by a physician:
  - Physical complaints like sore muscles, pain, headache, etc.
  - Reduced physical capacity, e.g. impairment in walking, cycling or at work
  - Psychological problems like increased levels of anxiety, depression or nervousness
  - Increased levels of fatigue
  - Sleep disturbances
  - Problems with coping with reduced physical and psychosocial functioning due to cancer.

Patients were not included if they met one of the following *exclusion* criteria:

- A very low level of activity, e.g. less than 50% of their time ambulant, rapid fatigue appearance after low physical activity performance, and ADL dependency
- Inability to travel independently to the rehabilitation centre

- Cognitive disturbances that may interfere with participation in the rehabilitation programme
- Emotional disturbances that may interfere with participation in the rehabilitation programme.

The Medical Ethics Committee of University Hospital Groningen approved the study. All patients provided informed written consent to participation in the study and for the procurement of medical information from their hospital charts. Medical data were verified by record linkage with the cancer registry of the Comprehensive Cancer Centre North-Netherlands.

Thirty-seven patients were included, but one patient left the programme for personal reasons and two patients did not finish the programme due to cancer recurrence. Therefore, data from the 34 patients who completed the programme at six weeks were taken for analysis.

### Rehabilitation programme

The rehabilitation programme took place in a rehabilitation centre. The programme took place with groups of 8–12 cancer patients in order to facilitate peer contact. The rehabilitation programme was approached from a multidisciplinary perspective and consisted of an intensive six-week multi-focus programme and a nine-week phase-out programme. During the intensive six-week programme, the sessions took place twice weekly, i.e., the group met 12 times, and the total number of contact hours was 46 hours.

The intensive rehabilitation programme consisted of the following components: (a) Individual Exercise, (b) Sports, (c) Psycho-education, and (d) Information.

#### **Individual exercise (twice a week, 1.5 hours)**

The exercise programme was divided into bicycle training and a muscle exercise circuit focussed on physical performance and muscle force respectively.

##### • *Bicycle training programme*

Patients exercised twice a week over the six weeks on a bicycle ergometer. Before the exercise training, a symptom-limited bicycle ergometry test was performed. This test was used as the basis on which an exercise schedule for individual patients was worked out, with two options: (1) in the case of physiological limitations during the ergometry test, for example the achievement of the heart rate predicted, the training programme was to be based on the training heart rate (THR), which was computed using the Karvonen formulae:  $THR = HR_{rest} + 50 \text{ to } 80\% (HR_{max} - HR_{rest})$  (Amundsen, 1979; Goldberg *et al.*, 1988; Karvonen & Vuorimaa, 1988). During weeks 1–3, exercise training was performed at a THR of  $HR_{rest} + 50 \text{ to } 60\% (HR_{max} - HR_{rest})$  and during

weeks 4–6 at a THR of  $HR_{rest} + 70$  to 80% ( $HR_{max} - HR_{rest}$ ). This aerobic exercise training was performed over 15–20 minutes with a warm-up before and a cool-down after the training. (2) In the case of symptom limitations without reaching physiological limitations due to severe symptoms, or for patients who could not reach a THR, the training was to be based on a protocol according to Alison (Alison & Anderson, 1981).

#### • *Muscle force training*

General muscle force training of the trunk and the lower and upper extremities was performed twice a week. Before training, the individual 1-Repetition Maximum (1-RM) was defined. Individual intensity of muscle force training started at 50% of the 1-RM during the first week, and was increased by 5–10% over the ensuing weeks with a frequency of 12 repetitions during three series. In the individual exercise programme, patients were also advised to follow a walking programme at home, once a week.

#### **Sports (twice a week, one hour)**

The sports programme consisted of sessions that were directed towards 'enjoying sports', 'self-confidence', and 'body knowledge'. In order to increase the chance that patients would continue sports activities in their leisure time after the end of the rehabilitation programme, patients were offered a variety of sports activities, like badminton, soccer, mini-golf, swimming, and so forth. During the performance of certain sports activities, patients were instructed to become aware of their physical sensations or limitations, in such a way that they would recognize and respect them in other sports.

#### **Psycho-education (once a week, two hours)**

The psycho-educational programme was aimed at reducing negative emotions and at improving coping with the disease. The psycho-educational programme was led by a course leader with several years experience in conducting group sessions with cancer survivors. The course leader brought up the following psychologically oriented topics with respect to cancer: 'confrontation with cancer', 'anxiety', 'stress', 'depression', 'asking for professional help', and 'social support'. Over several sessions, expressive-supportive techniques were used in order to explore negative emotions and to provide the opportunity to receive support from other cancer survivors. In addition, breathing exercises, relaxation exercises and exercises from Rational-Emotive Therapy were used in order to provide patients with stress-management techniques. Patients were instructed to practice the exercises and to prepare every session at home. All sessions were described in a course book that was used by course leader and participants.

#### **Information (once a week, one hour)**

The aim of the information programme was to reduce uncertainty due to lack of knowledge of the disease by providing information with respect to cancer-related subjects. Several professional healthcare providers who had specific knowledge of several subjects conducted the information session. The following subjects, with respect to cancer, were discussed in group sessions: 'medical aspects of cancer', 'cancer-related fatigue', 'food', 'sexuality', 'sport', 'body image', 'work and insurance', 'complementary medicine', 'pain', and 'daily activities'. During the session, patients were provided with information and were also given the opportunity to raise questions and to share experiences with other cancer survivors.

#### **Study design**

This study followed a prospective cohort study design. Measurements were performed before (T0) and at the end of the intensive six-week rehabilitation programme (T1).

#### **Outcome variables**

##### **Physical variables**

##### • *Physical capacity performance*

At T0 and T1 a symptom-limited bicycle ergometry test was performed using a ramp 10-, 15- or 20-protocol, depending on the patient's condition. This implied that the load was increased every minute by 10, 15 or 20 Watts respectively, in such a way that patients could reach their maximal workload within 10 minutes. The test was terminated on the basis of the patient's symptoms or at the physician's discretion (Wasserman *et al.*, 1987). Borg scores (Borg, 1982) for dyspnoea and muscle fatigue were taken before and after the test. Maximal workload, maximal  $O_2$  uptake,  $O_2$ -pulse and Borg scores at maximal workload were taken for analysis.

##### • *Muscle force*

Maximal voluntary isometric muscle force of the right and left extremity of extension of the knee, flexion of the knee, flexion of the elbow, extension of the elbow and grip-strength of the hand were measured using a hand held dynamometer (Force Evaluating & Testing [microFET], Hoggan Health Industries Inc, USA). The 'break method' was used for all measurements. To employ this technique, the examiner gradually overcame the force exerted by the patient until the extremity gave way (van-der-Ploeg & Oosterhuis, 1991). All measurements were performed at least three times, with recovery intervals of at least 10 seconds. The peak forces (in Newtons) were recorded and mean values of three technically correct measurements were taken for analysis. At that point, a compound value for general muscle force was calculated by computing a sum score of the values obtained for the upper and lower extremities to one sum value for each.

### Quality of life

Quality of life was measured with the RAND-36, the Rotterdam Symptom Check List (RSCL), and the Multi Fatigue Index (MFI). The RAND-36 is a multidimensional self-report questionnaire to assess global health-related quality of life. The questionnaire consists of the following nine domains: physical functioning (10 items), social functioning (two items), role impairment due to physical problems (four items), role impairment due to emotional problems (three items), mental health (five items), vitality (four items), pain (two items), general health appraisal (five items), and overall quality of life (one item). Scores range from 0 to 100 with a higher score representing better health. Psychometric characteristics of the instrument are described as follows: internal consistency ranges from  $\alpha = 0.71$ – $0.92$ ; test–retest is sufficient; the instrument has high convergent validity and low divergent validity (van-der-Zee and Sanderman, 1993). The RSCL is a self-report measure for the assessment of quality of life of cancer patients. The instrument is disease-specific and differentiates between disease and treatment state, and treatment processes. It consists of 39 items, which cover the following domains: physical symptom distress (23 items), psychological distress (seven items), activity level (eight items) and an overall valuation of quality of life (one item). Responses are given for most items on four-point Likert-type scale. A high score reflects a higher level of impairment burden. Psychometric characteristics of the instrument are described as follows: internal consistency is good; construct validity and clinical validity are sufficient (de-Haes *et al.*, 1996). The MFI is a self-report questionnaire that measures the following five aspects of fatigue: general fatigue (four items), physical fatigue (four items), reduction in activity (four items), reduction in motivation (four items), and mental fatigue (four items). Responses are given on four-point Likert-type scales. Scores range from 4–100, with a high score reflecting a greater sense of fatigue. Psychometric characteristics of the instrument are described as follows: internal consistency ranges from  $> 0.70$  to  $> 0.80$ ; construct and convergent validity are classified as good (Smets *et al.*, 1995; 1996).

### Statistical analysis

Statistical analyses were performed using the Statistical Package for the Social Sciences (SPSS). Non-parametric Wilcoxon tests were used for ordinal data and paired *t*-tests were used for interval and ratio data.

## Results

### Patient characteristics

Sixty-six percent of the patients were women with breast cancer (Table 1) and 70.2 % of the patients had a tumour at stage I or II. The most frequently mentioned indications for rehabilitation were reduced physical

**Table 1** Patients' characteristics at time of inclusion (T0) *n* = 37

|   |            |
|---|------------|
| Age, mean (SD), years   | 52.8 (6.2) |
| Range   | (43–67)    |
| Gender, male:female (%)                                       | 16.2:83.8  |
| Indication for rehabilitation (%)                             |            |
| Physical complaints   | 83.3       |
| Reduced physical capacity                                     | 94.6       |
| Psychological symptoms  | 78.4       |
| Fatigue   | 94.6       |
| Sleep disturbances  | 64.9       |
| Coping/acceptance problems                                    | 51.4       |
| Diagnosis (%)   |            |
| Breast cancer   | 67.6       |
| Non-Hodgkin lymphoma/M.Hogdkin                                | 8.1        |
| Gynaecological cancer   | 8.1        |
| Rest category (<5.0%)   | 16.2       |
| Stage (%)   |            |
| Stage I   | 24.3       |
| Stage II  | 45.9       |
| Stage III   | 21.6       |
| Stage IV  | 8.1        |
| Treatment before rehabilitation (%)                           |            |
| Surgical treatment  | 64.9       |
| Chemotherapy  | 62.9       |
| Radiotherapy  | 64.9       |
| Time between last treatment and programme start in months (%) |            |
| <6  | 29.7       |
| 6–12  | 32.4       |
| 12–18   | 16.2       |
| >18   | 21.6       |
| Median  | 7.1 months |

capacity (94.6%) and fatigue (94.6%). Within a year of their last cancer-related treatment, 61.2% of the patients started the rehabilitation programme. Thirty-four patients completed the intensive six-week programme, implying a dropout rate of 8.1%.

### Comparison T0 versus T1, outcome measurements

#### **Hypothesis 1: patients would do better physiologically after six weeks**

The immediate effects of the intensive rehabilitation programme on physical capacity and muscle force are presented in Table 2. Twenty-nine of the 34 patients performed the bicycle ergometry test and the hand-held dynamometry test at the end of the high-dose rehabilitation period. Two patients were not able to perform the test due to claustrophobia, nausea and absence, and three patients due to cancer-recurrence treatment. Statistically significant improvements were found in all physical outcome variables, including oxygen pulse, muscle force, and muscle fatigue (Tables 2 and 3), except for dyspnoea.

#### **Hypothesis 2: patients would report higher levels of quality of life after six weeks**

Tables 4, 5 and 6 present the prevalence of physical and psychosocial patient problems referred to the programme at time of inclusion, and the immediate effects of the rehabilitation programme on quality of life after six weeks. As expected, patients experienced more physical and psychological problems at the start of the programme than found in the general population (Tables 4, 5 and 6).

**Table 2 Descriptives of aerobic physical capacity and muscle force before (T0) and after six weeks of rehabilitation (T1), and paired t-tests**

|                                     | At T0, n=34 Mean (SD) | At T1, n=29 Mean (SD) | T      | p values |
|-------------------------------------|-----------------------|-----------------------|--------|----------|
| W. Max (W)                          | 112.2 (33.5)          | 124.8 (30.7)          | -3.908 | 0.001    |
| HR rest min <sup>-1</sup>           | 87.7 (13.6)           | 82.2 (10.9)           | 2.797  | 0.002    |
| Respiratory quotient                | 1.1 (0.1)             | 1.2 (0.1)             | -3.467 | 0.002    |
| O <sub>2</sub> -uptake (ml/min)     | 1389.5 (266.2)        | 1498.4 (392.2)        | -2.681 | 0.03     |
| O <sub>2</sub> -pulse (ml/hf)       | 10.0 (2.3)            | 10.7 (2.8)            | -2.588 | 0.02     |
| Muscle strength upper extremity (n) | 710.0 (150.9)         | 768.3 (190.1)         | -3.261 | 0.005    |
| Muscle strength lower extremity (n) | 544.9 (79.6)          | 620.7 (128.6)         | -3.430 | 0.001    |

**Table 3 Descriptives of Borg scores of dyspnea and muscle fatigue after bicycle ergometry force before (T0) and after six weeks of rehabilitation (T1), and Wilcoxon tests of the difference between scores at T0 and T1**

|  | T0 Median (range) | T1 Median (range) | p     |
|--|-------------------|-------------------|-------|
| Dyspnoea post-test (median, range)       | 3.0 (0.5-8.0)     | 3.0 (0.5-9.0)     | 0.150 |
| Muscle fatigue post-test (median, range) | 5.0 (0.0-8.0)     | 3.0 (0.5-7.0)     | 0.041 |

After six weeks of rehabilitation, patients showed a statistically significant improvement in physical functioning, role limitation due to emotional problems and vitality in the RAND-36 domains, as compared with baseline values (Table 4). Furthermore, the score on the change of health domain, which reflects a comparison between the present situation and the situation a year ago, was increased and reached a value which was greater than the mean score of the general population. In addition, patients in the study perceived a statistically significant reduction in physical symptom distress and psychological distress after six weeks following the rehabilitation programme (Table 5). Finally, patients experienced less general fatigue, physical fatigue and reduction in motivation after six weeks of the rehabilitation programme in comparison with baseline values on the MFI (Table 6). Change was not significant for the remaining RAND-36, RSCL and MFI domains.

## Discussion

The results of this study indicate that this intensive multi-focus rehabilitation programme for cancer patients is well tolerated and feasible. During the programme, three patients dropped out, two of them because of cancer recurrence, which is a dropout rate of only 8.1%.

Furthermore, the results of the study indicate that this intensive multi-focus rehabilitation programme had immediate short-term beneficial effects in cancer patients on physiological variables and on quality of life.

Our hypothesis that the intensive rehabilitation programme would result in physiological improvements within six weeks was confirmed. The most interesting finding of this study is that rehabilitation may lead to an increase in O<sub>2</sub>-pulse, which reflects genuine physiological training effects. Furthermore, the results of our study suggest that a six-week period is sufficient to achieve improvements in physical capacity variables, e.g., O<sub>2</sub>-pulse, O<sub>2</sub>-uptake and workload (Wmax). Very low values

for maximal O<sub>2</sub>-uptake, which were far below the norm values of maximal O<sub>2</sub>-uptake of 1600-2200 ml/min for untrained women (Schulz *et al.*, 1998), were found at intake. After six weeks of rehabilitation we found an increase in O<sub>2</sub>-uptake, although normal values for healthy untrained women were not attained. These results are in agreement with the Schulz study (Schulz *et al.*, 1998). An improvement in physical performance after an exercise program was also found by Dimeo in several small groups of patients (Dimeo *et al.*, 1996; 1997; 1998). However, in those studies, physical performance was indirectly assessed by calculating metabolic equivalents (METs), which is less accurate (Dimeo *et al.*, 1997) and may lead to misinterpretations (Wasserman *et al.*, 1987). Additionally, in this study, lower Borg scores for muscle fatigue post-test were obtained, which reflect a reduction in fatigue experienced after the bicycle test. In general, based on the physical improvements, it can be concluded that patients achieved a higher workload with less subjective and objective effort after six weeks of intensive rehabilitation.

The hypothesis concerning improvement in quality of life following the intensive multi-focus high-dose rehabilitation programme was confirmed in several of the global and disease-specific quality of life domains, and in fatigue. Patients experienced an improvement in physical functioning and vitality after six weeks of rehabilitation. These improvements may have been due to a positive transfer effect of increased physical capacity. This is in agreement with earlier studies reporting an increased physical capacity (VO<sub>2</sub>max) and an improvement in the same RAND-36 domain in women with breast cancer who participated in an exercise programme (Schulz *et al.*, 1998; Segal *et al.*, 2001).

The scores in the physical functioning and physical symptom distress (RSCL) domains were statistically significantly improved after the intensive programme, while for the scores in the role limitation due to physical

**Table 4** RAND-36 scores for general population (van-der-Zee & Sanderma, 1993), patients at T0, patients at T1, and Wilcoxon test of the differences between scores at T0 and at T1

|                                     | General population <i>n</i> =1063<br>Mean (SD) | Patients at T0 <i>n</i> =37 Mean (SD) | Patients at T1 <i>n</i> =34 Mean (SD) | <i>p</i> values |
|-------------------------------------|--|---------------------------------------|---------------------------------------|-----------------|
| Physical functioning                | 81.9 (23.9)                                    | 58.2 (20.3)                           | 62.1 (20.0)                           | 0.029           |
| Social functioning                  | 86.9 (20.5)                                    | 55.7 (19.7)                           | 60.0 (25.2)                           | 0.196           |
| Role limitation (physical problem)  | 79.4 (35.5)                                    | 20.7 (32.9)                           | 28.0 (32.4)                           | 0.162           |
| Role limitation (emotional problem) | 84.1 (32.3)                                    | 34.2 (40.0)                           | 51.0 (44.4)                           | 0.036           |
| Mental health                       | 76.8 (18.4)                                    | 59.9 (17.8)                           | 63.8 (18.3)                           | 0.126           |
| Vitality                            | 67.4 (19.9)                                    | 45.6 (18.9)                           | 49.9 (20.1)                           | 0.049           |
| Pain                                | 79.5 (25.6)                                    | 67.5 (20.8)                           | 68.3 (21.2)                           | 0.499           |
| General health appraisal            | 72.7 (22.7)                                    | 52.6 (13.8)                           | 53.2 (15.7)                           | 0.697           |
| Change of health                    | 52.4 (19.4)                                    | 43.3 (38.2)                           | 61.8 (38.6)                           | 0.010           |

**Table 5** RSCL scores for general population (de-Haes *et al.*, 1996), patients at T0, patients at T1, and Wilcoxon tests of the differences between scores at T0 and at T1

|                           | General population <i>n</i> =201<br>Mean (SD) | Patients at T0 <i>n</i> =37 Mean (SD) | Patients at T1 <i>n</i> =34 Mean (SD) | <i>p</i> values |
|---------------------------|---|---------------------------------------|---------------------------------------|-----------------|
| Overall valuation of life | 21.1 (83.7)                                   | 38.9 (16.9)                           | 40.6 (20.7)                           | 0.599           |
| Psychological distress    | 17.0 (18.1)                                   | 37.3 (21.2)                           | 30.1 (20.7)                           | 0.015           |
| Physical symptom distress | 9.9 (9.0)                                     | 24.5 (10.2)                           | 22.5 (11.8)                           | 0.031           |
| Activity level            | Not available                                 | 21.5 (22.2)                           | 19.8 (16.9)                           | 0.656           |

**Table 6** MFI scores for general population (Smets *et al.*, 1998), patients at T0, patients at T1, and Wilcoxon tests of the differences between scores at T0 and at T1

|                         | General population <i>n</i> =139 | Patients at T0 <i>n</i> =37 | Patients at T1 <i>n</i> =33 | <i>p</i> values |
|-------------------------|----------------------------------|-----------------------------|-----------------------------|-----------------|
| General fatigue         | 9.91 (5.2)                       | 15.5 (3.6)                  | 14.4 (4.2)                  | 0.024           |
| Physical fatigue        | 8.79 (4.9)                       | 15.1 (4.1)                  | 13.1 (4.3)                  | 0.007           |
| Reduction of activity   | 8.69 (4.6)                       | 12.7 (4.5)                  | 12.0 (4.4)                  | 0.159           |
| Reduction of motivation | 8.23 (4.0)                       | 10.4 (3.6)                  | 9.8 (3.9)                   | 0.013           |
| Mental fatigue          | 8.33 (4.8)                       | 12.8 (4.0)                  | 13.8 (4.7)                  | 0.824           |

problems in the RAND-36 domain, only a trend of improvement was found. This may indicate that role limitation is affected in the long term.

Another interesting finding in this study was the significant reduction in psychological distress. This finding is in agreement with another study (Dimeo *et al.*, 1999) that concluded that aerobic exercise might improve psychological distress. In the present study, the decrease in psychological distress may be explained by the following. Firstly, the decrease may be the result of the psychosocial or educational components of the intervention. Secondly, a transfer effect from improved physical to improved psychological functioning may have occurred, i.e., improvement in physical performance may have increased the patients' sense of control, independence, self-esteem and self-efficacy (Dimeo *et al.*, 1999). Thirdly, the decrease may have been a result of non-specific effects of attention.

Fatigue is the most frequently reported side effect in cancer patients, but its determinants and consequences are still largely unexplored (Visser and Smets, 1998). In

this study, several improvements were found in fatigue experienced after six weeks of rehabilitation, especially in 'general' and 'physical' fatigue. This decrease in fatigue may have been due to improved physical capacity and muscle force. Furthermore, patients demonstrated less reduction in motivation, which may have resulted from their lower levels of reported psychological distress. The 'reduction of activity' and 'mental fatigue' domains remained unchanged. These results could suggest that improvement in physical capacity may at first have resulted in improvement of general and physical fatigue and less reduction in motivation, and that in order to obtain less reduction in activity and mental fatigue, a further increase of  $\text{VO}_2\text{max}$ , or some other factors, is necessary.

Our hypothesis that the intensive multi-focus programme would result in positive effects on quality of life (including fatigue) was confirmed in nine of 18 domains. However, it remains unclear which components of the programme were responsible for the improvements achieved in physical, psychological and social quality of life. With respect to the physiological improvements, it

may be assumed that these may have been due to the physical component of the programme, since physiological improvements only occur due to certain training principles (Goldberg *et al.*, 1988) and not as a result of 'social support' by peers or psychosocial or educational interventions.

The results of this study may contribute to the knowledge of cancer rehabilitation. Although further research is necessary, the effects obtained, both on physiological functioning and on quality of life within six weeks, can be used for further development of cancer rehabilitation programmes.

### Study limitations and future recommendations

Although the programme was open to a mixed group of cancer patients, more than half of the participants were women with breast cancer, which may limit the generalisability of the results of our study. Most patients had a cancer at stage I or II, which may reflect the relatively good prognosis of the patients who were referred to the programme. Although this may indicate the correct use of the inclusion criterion of a life expectancy of more than a year, it shows that the results of this study may not be generalisable to the whole population of cancer patients. At the same time, however, these patients form exactly the target population for cancer rehabilitation programmes that focus on improvement and recovery.

Based on the high level of physical and psychological problems encountered, it should be noted that the group of patients in this study might not be representative of cancer patients in general. This is supported by an earlier study showing that programme participants perceive more physical and psychological symptoms than patients who choose not to participate into a rehabilitation programme (Berglund *et al.*, 1993) (van-Harten *et al.*, 1998). Therefore, the poor quality of life found in our group of patients may also be the result of the inclusion criteria used for the study.

A final limitation to our study is that we did not include a control group. Therefore, the results of our study should be interpreted with care. Future research should use a randomised controlled trial design in order to determine the effects of the various components of the programme.

### Acknowledgements

This study was supported by a grant from the Dutch Rotary and Dutch Cancer Society.

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